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DRAWINGS ATTACHED

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(54) METHOD OF MAKING MULTI-WALL CAPSULES

(71) We, FUJI PHOTO FILM CO., LTD., a Japanese Company, of 210, Nakanuma, Minami-Ashigara-Machi, Ashigara-Kamigun, Kanagawa, Japan, do hereby declare the invention for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement: —

This invention relates to a method of making multi-wall capsules in which a double or triple coating wall film is formed on a single wall film.

The term "single-wall capsule" means a capsule having a size of a fraction of a micron to several centimetres and consisting of one or more cores coated once only with a wall-forming material. Methods of making microcapsules are disclosed in detail in "Yakuzaigaku (Pharmacology)", Vol. 26 (1966, pp 1—7. Capsules having a size of one millimeter to one centimetre can be made according to the methods of U.S. Patents Nos. 3,190,837 and 3,341,466, and Japan Patent Publication No. 6799/1968.

Such a single-wall capsule is insufficient in strength and in permeability, and must therefore be strengthened. To this end, the single-wall capsule is preferably coated double or triple. Multi-wall capsules are known as shown in Japanese Patent Publications Nos. 13681/1967, 2329/1967 and 20467/1967, and another capsule structure is disclosed in Japanese Patent Publication 1881/1963 in which a number of single-wall capsules are further encapsulated as a core.

We have now found a new method of forming double or triple wall films on single-wall capsules by utilizing the phenomenon that an aqueous solution of a water-soluble high molecular material having hydroxyl, acid or basic groups can be reacted with an aqueous solution of a hardener such as an inorganic polyvalent metal ion, alkali, acid or salt to thus rapidly form an insoluble film in water.

As used herein, the term "multi-wall capsule" means "a capsule formed by encapsulation of one or more other capsules which may be single- or multiple-walled and single or multiple cored".

According to the invention, a method of making multi-wall capsules as herein defined comprises dispersing in an aqueous solution of a water-soluble high molecular film-forming material having hydroxyl acid or basic groups, single-wall capsules, each of which contains a nucleus or nuclei therein, and then adding the resulting dispersion to an aqueous solution of a hardener for said water-soluble high molecular material.

The method of the invention may be carried out as follows. Throughout the specification, all percentages are by weight. Single wall capsules are dispersed in an aqueous solution of a water-soluble high molecular material having a concentration of several tenths to several tens %. When the resulting dispersion is formed, for example, by a nozzle or centrifugal force into a liquid drop of desired size and dropwise added to an aqueous solution of an appropriate hardener having a concentration of 1/20% to 30%, double wall capsules are formed, and these are recovered by a suitable method and dried. When the thus obtained double wall capsules are dispersed in an aqueous solution of the same or a different water-soluble high molecular material and the procedure is repeated, triple wall capsules are obtained.

A preferred preparation of the multi-wall capsule of the invention is carried out as follows. Oil-containing single wall capsules in which the wall film consists of a complex coacervate of gelatin and gum arabic (made by the method according to U.S. Patent No. 2,800,457 or Japanese Patent No. 493,064) are recovered as a thickened capsule slurry by filtering or decantation and are dispersed in an equal volume of a 2% aqueous solution of sodium alginate. A 10% aqueous solution of calcium chloride is selected as a hardener and

stirred. The aforesaid capsule dispersion is added to the hardener in the form of liquid drops having a desired size of several tens of microns to several millimeters, thereby obtaining instantaneously substantially spherical double-wall capsules. When the capsule dispersion is extruded into the hardener through a nozzle having a certain diameter, rod-shaped double-wall capsules are obtained.

Examples of water-soluble high molecular materials suitable as wall forming materials in carrying out the invention and of appropriate hardeners therefor are shown in the following Table. Above all, sodium alginate hardener by Ca^{++} ions and polyvinyl alcohol are preferred materials because of their very rapid hardening reaction and high film strength.

TABLE

Water-soluble high molecular material	Hardener
sodium alginate	Ca^{++}, Al^{+++}, acid
carageenin	Ca^{++}
dextran and other sulphuric acid esters	Ca^{++}, Ba^{++}
Glucomannan	Ca^{++}, alkali
carboxymethyl cellulose carboxymethyl starch	Al^{+++}, Fe^{+++}, Cu^{++}
acid-soluble collagen	alkali
polyvinyl alcohol	borax
copolymer of polyvinyl methyl ether and maleic anhydride	Fe^{+++}
agar	tannic acid (with cooling)
milk casein	Ca^{++}, acid
Chitosan oxalate	alkali

The important feature of the multi-wall capsule made according to the method of the invention lies in that its surface is not sticky not only in water but also as it is removed from water, that is, in the undried state, resulting in a convenience of handling. Many of the single wall capsules, in particular those formed by phase separation from an aqueous system, have the disadvantage that the capsule surface is too sticky to give the following dry powder immediately after they are made. The method of the invention can favourably be adapted thereto with such advantages as strengthening the capsule and giving readily a dry powder.

The multi-wall capsule of the invention will now be illustrated with reference to the accompanying drawing in which Figs. 1 to Fig. 4 are schematic illustrations of some embodiments of capsules according to the invention:

Fig. 1 shows one embodiment of the invention, a double wall capsule 5 wherein an oil droplet 1 as a core is coated with a coacervate 2 to give a single-wall capsule 3 and is further coated with calcium alginate 4.

Fig. 2 shows another embodiment of the invention, a double wall capsule 5 wherein a plurality of oil drops 1 are coated with a coacervate 2 to give a single-wall, multi-cored capsule 3 and further coated with calcium alginate 4.

Fig. 3 shows a further embodiment of the invention, a triple wall capsule 6 wherein a number of single-wall capsules 3 having single or multiple cores are together coated with a first layer of calcium alginate 2 to give a double-wall capsule 5 and further coated with another layer 2 of calcium alginate.

Fig. 4 shows a still further embodiment of the invention, a rod-shaped double-wall capsule 5 containing a number of single-wall (single- or multi-cored) capsules 3.

The following examples are given in order to illustrate the invention.

EXAMPLE 1

15 g of a dibutyl phthalate solution containing 35% of menthol were emulsified in 100 ml of 2% aqueous solution of sodium alginate in a size of 0.1—2 mm. The dibutyl phthalate

emulsion was dropwise added to a 5% aqueous solution of calcium chloride with agitation through a glass tube 5 mm in diameter, whereby to form single wall spherical capsules of 3—4 mm in diameter. The aqueous solution of hardener was removed by decantation and the capsules were washed with water for 1 or more hours in flowing water. Since the encapsulation was insufficient, the dibutyl phthalate was found exuded on the capsule film after drying.

Double wall formation: 15 g of the above mentioned single-wall capsules were dispersed in 80 ml of 2% aqueous solution of sodium alginate. The dispersion was dropwise added to a 7% calcium chloride solution through a glass tube 6 mm in diameter. The single wall capsules will further coated with calcium alginate to form a double-wall capsule. The resulting double-wall capsules were washed with water, collected in a basket and then dried. Although there was some smell of menthol, the wall film surface was completely dry and there was found no exuding of the dibutyl phthalate solution, before the capsule was pressed by a finger.

Triple wall formation: The foregoing double-wall capsules were wetted with a 10% aqueous solution of polyvinyl alcohol, dropwise added to a saturated aqueous solution of borax at normal temperature, recovered and washed with water to give triple-wall capsules the outside wall of which consisted of a complex film of polyvinyl alcohol and borax. The resulting capsules were very strong and free from any menthol smell.

EXAMPLE 2

Single wall capsules of 20—50 microns having a wall film of a gelatin gum arabic coacervate and containing silicone oil were made according to the method disclosed in U.S. Patent No. 2,800,457. A slurry of this capsule was dispersed in the same volume of a 1.8% aqueous solution of sodium alginate. The resulting single-wall capsule dispersion was dropwise added to 8% aqueous solution of calcium chloride in the form of liquid drops of about 5—6 mm in diameter, recovered and washed with water to obtain double-wall capsules containing silicone oil.

WHAT WE CLAIM IS:—

1. A method of making multi-wall capsules as hereinbefore defined, which comprises dispersing in an aqueous solution of a water-soluble high molecular film-forming material having hydroxyl, acid or basic groups, single-wall capsules, each of which contains a nucleus or nuclei therein, and then adding portions of the resulting dispersion to an aqueous solution of a hardener for said water-soluble high molecular material.

2. A method as claimed in claim 1 wherein said water-soluble high molecular material is sodium alginate and said hardener comprises calcium ions.

3. A method as claimed in claim 1 wherein said water-soluble high molecular material is polyvinyl alcohol and said hardener is borax.

4. A method as claimed in claim 1 wherein the water-soluble high molecular material and the hardener are any of those pairs thereof shown in the table herein.

5. A method as claimed in claim 1 wherein said single-wall capsule has a wall of a complex coacervate of gelatin and gum arabic which is produced by coacervation.

6. A method as claimed in any preceding claim, wherein the thus obtained capsules are again dispersed in an aqueous solution of the same or a different water-soluble high molecular film-forming material having hydroxyl, acid or basic groups, the resulting dispersion is added to an aqueous solution of a hardener for said water-soluble high molecular material and, if desired the procedure is repeated.

7. A method of making multi-wall capsules, substantially as herein described with reference to either of the foregoing Examples.

8. Multi-wall capsules produced by a method according to any preceding claim.

9. Multi-wall capsules according to claim 8, substantially as hereinbefore described with reference to any of the Figures of the accompanying drawings.

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FIG. 1

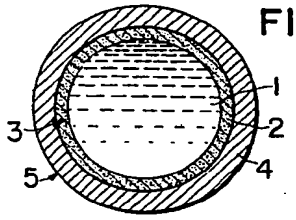

FIG. 2

FIG. 2

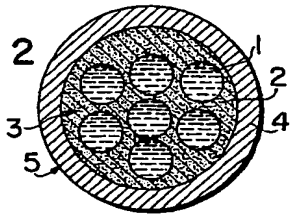

FIG. 3

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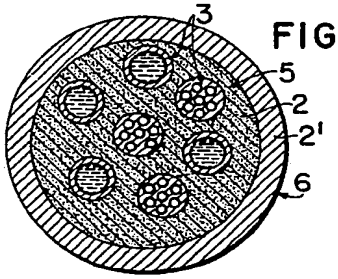

FIG. 4